

## DISCUSSION

The cases presented here are unusual in that there was no history or clinical evidence of a bite by a rat or other animal. Furthermore, both patients recovered completely without chemotherapy. Inasmuch as there were few symptoms, the principal findings were serologic. An agglutination of 1:80 against the prepared phenolized antigen is considered significant.

In recent years treatment with penicillin has been found efficacious.

## SUMMARY

Two cases of ratbite fever due to *Streptobacillus moniliformis* were proved by positive reaction to serologic tests. These are the first cases of this disease to be reported from Los Angeles County. Recovery was uneventful without specific therapy.

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## Simultaneous Occurrence of Squamous and Adenocarcinoma of the Lung

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INSTANCES of multiple primary carcinomas can be found in most large tumor registries. To establish this diagnosis, the tumors must differ histologically, must arise in different locations and must be the source of metastatic lesions. In most reported cases of multiple primary carcinomas, only the first two criteria are met.<sup>9,11</sup> The present report describes an example of a relatively infrequent coincidence of lesions—double primary bronchogenic carcinoma\*—and demonstrates the difficulties of determining which of two coexistent lung lesions is malignant.

## REPORT OF A CASE

A 77-year-old white man entered the hospital because of cough, shortness of breath, fatigue, lethargy, weakness, anorexia, loss of 30 pounds of weight and swelling at the ankles, all of three months' duration. He had no history of exposure to industrial irritants or to tuberculosis. He had smoked one package of cigarettes daily for 50 years.

On physical examination, the patient appeared acutely and chronically ill. The temperature was 98°F., the pulse rate 140 and respiration 36 per minute. The blood pressure was 100/70 mm. of mercury. There was no cyanosis of the skin or mucous membrane and no clubbing of the fingers or toes. In the sitting position, his neck veins were distended. The anterior-posterior diameter of the

chest was greater than normal. Respiratory movements on prolonged expiration were decreased. The lungs were dull to percussion over both apices. Hyperresonance to percussion was noted over the lower one-third of the chest anteriorly and posteriorly. Musical and subcrepitant rales were heard throughout both lungs. The cardiac impulse was not seen or felt, and the cardiac border could not be percussed. The cardiac rhythm was regular and rapid, and no murmurs were heard. The liver was tender to palpation, and the edge was felt 7 cm. below the right costal margin. No shifting dullness or fluid wave was elicited in the abdomen. Pitting edema in the lower extremities and extending to the sacral region was noted.

A roentgenogram of the chest (Figure 1) showed flattened leaves of the diaphragm bilaterally and increased radiolucency of both lung fields. An oval density in the left apex contained a radiolucent area, suggesting a cavity. An infiltrative process was present in the apex and first anterior interspace of the right lung.

Reaction to a tuberculin skin test was positive; to histoplasmin and coccidioidin skin tests, negative. Smears and cultures of the sputum were negative for tubercle bacilli. In cytologic study of the sputum, bizarre hypercornified, multinucleated hyperchromatic cells were observed. Bronchoscopic examination revealed no abnormalities. Specimens taken from the left and right bronchial trees were unsatisfactory for cytologic study. No pathologic changes were noted on biopsy of specimens from the right and left scalene lymph nodes.

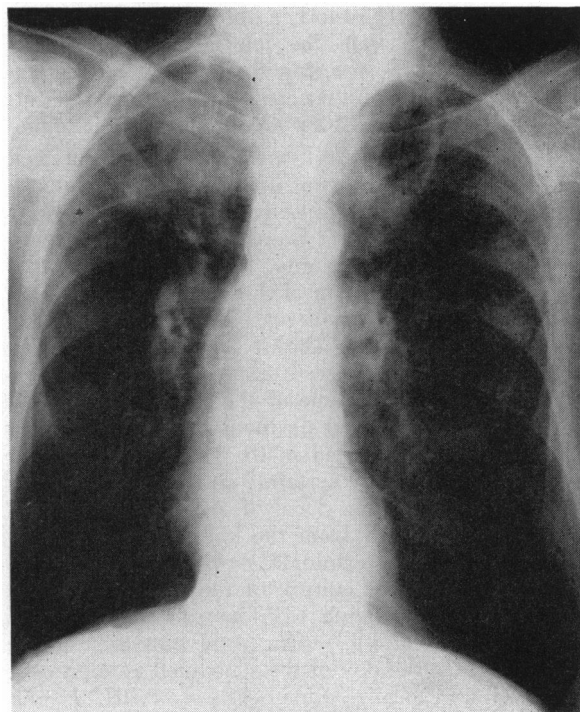


Figure 1.—Posterior-anterior roentgenogram of chest showing lesions in the right and left upper lobes.

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\*References 1, 3-8, 10.

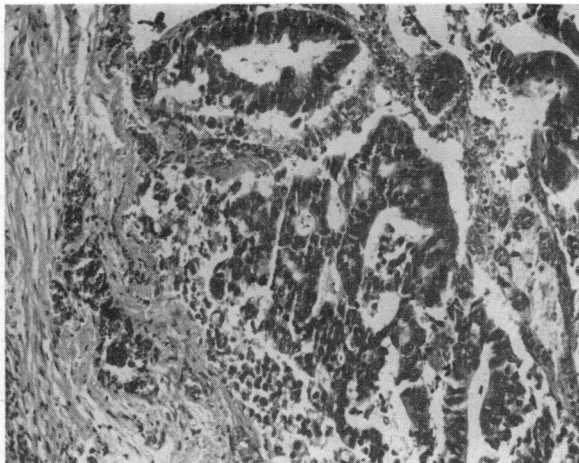


Figure 2.—Photomicrograph from apex of right lung showing adenocarcinoma with gland formation ( $\times 250$ ).

The attending staff thought that the lesion in the right lung was a squamous cell carcinoma and that that in the left lung was caused by tuberculosis. Because of the patient's age and condition, thoracotomy was not advised, and he was treated with isoniazid and streptomycin. Monthly roentgenograms of the chest revealed no significant changes. Malignant cells of the same type as before were found on repeated cytologic examinations of the sputum. The patient was given 20 mg. of nitrogen mustard on three occasions without noticeable improvement. He did poorly, had several episodes of hemoptysis and died seven months after hospitalization.

#### **PATHOLOGIC EXAMINATION**

The pleural cavities were free of fluid and the lungs were expanded. The right lung weighed 625 gm. The right upper lobe contained an irregular firm region that extended from the hilum to the apex. On cut surface it appeared as a grey-brown mottled consolidated tissue. A firm grey thrombus occluded the artery in this region. The cut surfaces of the right middle and lower lobes were red and congested and oozed fluid. The bronchi in this region were reddened and contained grey mucoid secretions. The left lung weighed 575 gm. At the apex was a cavity into which projected polypoid tumor tissue arising from the bronchus supplying that portion of the lobe. Dark red areas of soft consistency were observed on cut surfaces of the upper and lower lobes. The remainder of the parenchyma was firmer, less red and not crepitant. The hilar and mediastinal lymph nodes were dark in color and contained small scarred areas that obscured the normal structure.

Microscopic examination of sections from the apices of each lung showed infiltration by tumor tissue surrounded by areas of fibrosis and necrosis. Tissue from the right lung (Figure 2) showed papillary and glandular patterns composed of cells with hyperchromatic, pleomorphic nuclei and dense

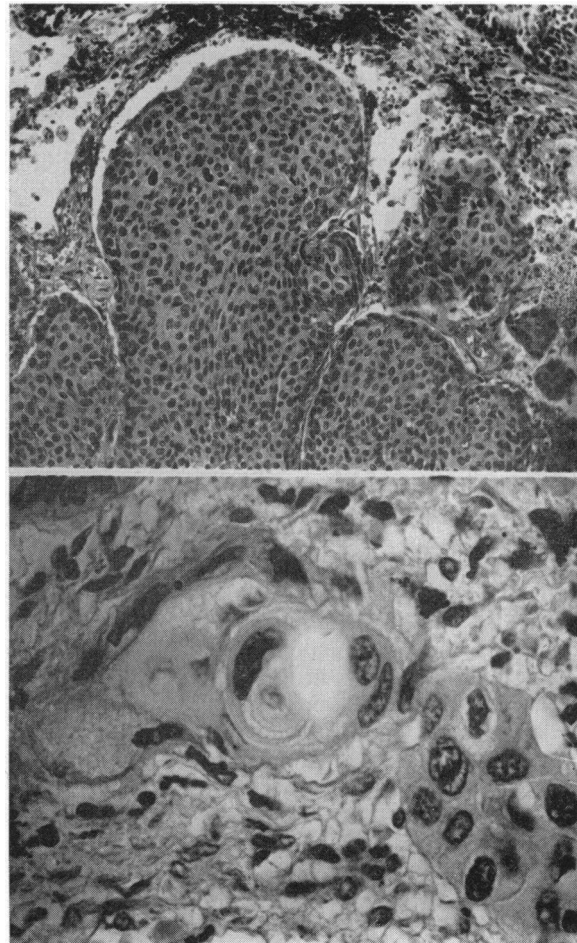


Figure 3.—*Top*: Photomicrograph from apex of left lung showing a squamous cell carcinoma ( $\times 250$ ). *Bottom*: Photomicrograph from another portion of the tumor showing epithelial pearl formation and intercellular bridge formation ( $\times 800$ ).

pink cytoplasm. There was mucus formation by the tumor. The tumor had involved the wall and obliterated the lumen of a large bronchus. Tissue from the left lung (Figure 3) showed malignant epithelium in sheets and strands differentiated toward the squamous cell type with some palisading at the margins and keratinization. Epithelial pearl formation and intercellular bridging were present in portions of the tumor. The nuclei were large and pleomorphic and contained irregularly clumped chromatin. The tumor supplanted the mucosa of a fairly large bronchus. Sections from both lungs showed congestion with focal edema, atelectasis and emphysema. No other tumor sites in either lung, or extrapulmonary tumor metastasis or other primary tumors, were found.

The final diagnoses were: Bronchogenic carcinoma (adenocarcinoma upper lobe of right lung, squamous cell carcinoma upper lobe of left lung); pulmonary edema and congestion; pulmonary emphysema; and thrombosis of medium-sized artery in upper lobe of right lung.

## DISCUSSION

The incidence of multiple simultaneous unilateral or bilateral lung carcinoma is not known. Relatively few such instances have been reported, and some of these are doubtful because of the difficulties in distinguishing primary from metastatic lesions. Cahan and co-workers,<sup>2</sup> in a study of 1,493 patients with bronchogenic carcinoma, found 25 coexistent primary carcinomas, but no instance of double primary lung tumors. Warren and Gates<sup>11</sup> in a study of reports of multiple malignant lesions noted that the reported incidence varied from 1.84 to 3.9 per cent. Of the 1,259 cases of multiple malignant lesions cited, none were cases of double primary bronchogenic tumors. Slaughter<sup>9</sup> noted only three instances of multiple lung tumors in 1,868 reported cases of multiple malignant lesions. In 234 cases of bronchogenic carcinoma, Olcott<sup>6</sup> found only one instance in which presumptive evidence indicated a double primary lung carcinoma. Robinson and Jackson<sup>7</sup> reported double bronchogenic carcinomas in 9 of 500 patients with bronchogenic carcinoma, the largest number reported by one group of investigators. The authors stated the number of cases in the series was too few in number to be statistically significant. McGrath and co-authors<sup>5</sup> found five instances of grossly visible double tumors in the same or different lobes in 87 cases of bronchogenic carcinoma. Other reports have described double primary bronchogenic carcinomas in the same or opposite lungs.<sup>1,3,4,8,10</sup>

The premortem diagnosis of bronchogenic carcinoma in the present case was made on the basis of cytologic studies of the sputum. The roentgenographic evidence of a lesion in the apex of each lung raised the possibilities that one was malignant and the other not, that one was metastatic from the other, that both were themselves metastatic from an extrapulmonary site or that one was a primary and the other metastatic from an extrapulmonary site. Despite bronchoscopic examination with attempts to obtain secretions independently from each lung, despite biopsy of the scalene lymph nodes and use of antituberculous therapy and nitrogen mustard, the location of the tumor was not known before death. At necropsy, two circumscribed and well differentiated tumors were found: An adenocarcinoma in the right lung and a squamous cell carcinoma in the left. No nearby or distant metastatic lesions from either tumor or another primary tumor were found. These findings meet two of the three criteria for the diagnosis of multiple primary tumors; while it cannot be proved, the supposition that the tumors were independent appears supportable.

The dilemma raised by lesions in both lungs in cases in which diagnosis of bronchogenic carcinoma is established is difficult to resolve. If one lesion is metastatic from the other, thoracotomy is not warranted. If only one lesion is malignant, the wrong side may be explored. Although few patients with bronchogenic carcinoma survive five years, even this

small chance for survival must not be denied a patient considered to have (but who actually does not have) a metastatic lesion.

The microscopic appearance of bronchogenic carcinomas is not uniform.<sup>5,6</sup> Different cell types are often found within the primary lesion, and the cell type in the primary may differ from that in metastatic sites. This lack of uniformity may result from the coalescence of tumor from many sites.<sup>5</sup> Nevertheless, a relatively well-differentiated squamous cell carcinoma would not be expected to give rise to a well-differentiated adenocarcinoma, or vice versa. It is probable that the two tumors in the present case were independent and were coincident by chance.

## SUMMARY

A case in which an adenocarcinoma in one lung was found to coexist with a squamous cell carcinoma in the other lung is reported—apparently a case of double primary unrelated pulmonary malignant lesions. The report demonstrates the difficulties in determining which lung is involved when both show lesions and where the diagnosis but not the site of the bronchogenic carcinoma has been established.

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